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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,398	08/03/2000	ABDESSATAR CHTOUROU	065691/0193	9759

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,398	CHTOUROU ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,25,29,31-34,36,37,39-49 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29,31-34,39-49 and 51* is/are rejected.

7)☒ Claim(s) *24,25,36 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/9/2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/9/04 has been entered.

ACKNOWLEDGMENT OF AMENDMENT, REMARKS AND STATUS OF THE CLAIMS

2. The amendment, remarks filed on 4/9/04 are acknowledged, entered and considered. In view of Applicant's request claims 24, 25, 29, 31-34, 39-49 and 51 have been amended and claims 26-28, 30, 35, 38 and 50 have been canceled. Claims 24, 25, 29, 31-34, 36, 37, 39-49 and 51 are now pending in the application. The rejections under 35 U.S.C. 112, second paragraph and 35 U.S. C. 103(a) over the prior art of record are withdrawn in view of Applicant's amendment, cancellation of claims and remarks filed 4/9/04. However, the rejection for claim 51 under 35 U.S.C. 103(a) is maintained for the reasons of record because claim 51 is a product-by-process claim.

CLAIM REJECTIONS-35 U.S.C. § 103(a)

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 51 remains rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/00237 taken with Josic et al. (J. Chromatogr. B. Biomed. Appl., Vol. 662, No. 2, pp. 181-190, 1994), Grandgeorge et al (U.S. Patent No. 5,371,195) and Farb et al (U.S. Patent No. 4,758,657).

Claim 51 is in product-by-process format. The novelty and patentability of the claimed product is based on the claimed procedure and not on the recited process steps. Claim 51 recites (even as dependent on claim 24) no new novel properties

based on the claim 24 recited processes. The cited primary reference of WO 96/00237 teaches that the old product have been expected by one of ordinary skill in the art to have been filtered by a filtration step using a filter with a porosity of 15 nm for the intended purpose of reducing the content of very small non-enveloped viruses, such as parvoviruse, polio virus, hepatitis virus, etc. (See e.g., page 7, lines 30 to page 9, lines 27). Further the secondary reference of Josic et al. teach the dissociation complex of FVIII and vWF by adding calcium ions and Grandgeorge et al (U.S. Patent No. 5,71,195) teaches a method for purifying FVIII from cryoprecipitate. Thus, claim 51, the claim is in product-by-process format and as such, it is the novelty and patentability of the instantly claimed product that need be established and not the recited process steps, In re Brown, 173 USPQ 685 (CCPA 1972); In re Wertheim, 191 USPQ (CCPA 1976). Further, the prior art described the product as old, In re Best, 195 USPQ 430, 433 (CCPA 1977); (See MPEP 706.03 [e]). Hence, the burden of proving that the process limitation makes a different product is shifted to the Applicants, In re Fitzgerald, 205 USPQ 594.

NEW GROUNDS OF REJECTION

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 29, 31-34 and 39-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite in the recitation "The method according to claim 24, wherein the $CaCl_2$ is added in the form of a saline solution of 0.2 M to salt saturation." Because in claim 24 $CaCl_2$ is present in a solution, and as such, it is inconsistent with claim 24 by reciting "$CaCl_2$ is added. Further, the term "salt" is superfluous. Amendment of the claim to recite "The method according to claim 24, wherein the $CaCl_2$ is present in the solution from 0.2 M to saturation" is suggested.

Claim 31 is indefinite for the same reasons discussed under claim 29. Further claim 31 depends on cancelled claim 28. Thus, amendment of the claim to recite "The method according to claim 24, wherein the $CaCl_2$ is present in the solution from 0.35 M to saturation" is suggested.

Claim 32 is indefinite and confusing in the recitation "... a pressure lower than the threshold recommended by the supplier" because it is not clear what is meant by a pressure lower than the threshold recommended by the supplier since claim 24 recite "a pressure of less than 0.3 bar" and as such it is obviated by claim 24. Deletion of dependent claim 32 is suggested.

Claim 33 is redundant in the recitation "wherein the filter has a pore size of 15 nanometers" because the pore size of 15 nm has already been recited in independent claim 24. Deletion of claim 33 is suggested.

Claims 39 and 40 are indefinite and confusing as currently drafted because claim 39 depends on independent claim 24 and recites "...wherein the starting factor VIII solution is obtained by heparin precipitation" while claim 40 depends on claim 39 and recites "...wherein the starting factor VIII solution of (a) is derived from a

cryoprecipitated fraction of plasma". However, according to the instant specification on pages 6 and 7, and particularly on page 7, lines 31-38 clearly states that "...a cryoprecipitated fraction of the plasma is absorbed...in the presence of heparin.....". Thus, the first step, which occurs, is the cryoprecipitation and then heparin precipitation. Amendment of claim 39 to recite " The method according to claim 40, wherein the starting factor VIII solution is obtained by a further heparin precipitation" and claim 40 to recite " The method according to claim 24, wherein the starting factor VIII solution of (a) is derived from a cryoprecipitated fraction of plasma" is suggested.

Claim 26 is grammatically indefinite in the recitation ".... An anti-viral solvent or detergent, or both". Amendment of the claim to recite "an anti-viral solvent, a detergent, or both" is suggested.

Claim 24 is indefinite in the recitation " wherein the stating factor VIII is immunopurified" because the claim is inconsistent with claim 24 which recites "factor VIII solution". Amendment of the claim to recite "wherein the stating factor VIII solution is immunopurified" is suggested.

Claim 43 is indefinite in the recitation ".....comprises recombinant factor VIII." Amendment of the claim to recite ".....comprises recombinantly produced factor VIII." Is suggested.

Claim 46 recites the limitation "wherein the concentration" in lines 1 and 2. There is insufficient antecedent basis for this limitation in claim 46 or claim 24.

Claim 48 recites the limitation "wherein the protein content" in lines 1 and 2. There is insufficient antecedent basis for this limitation in claim 48 or claim 24.

OBJECTION TO THE CLAIM

5. Claim 24 is objected in the recitation the acronym "factor VIII-vWF" in step (a). Use of full terminology i.e., factor VIII-von Willebrand factor (FVIII-vWF) at least in the first occurrence would obviate this objection.

CLAIMS REJECTION-35 U.S.C. § 112 FIRST PARAGRAPH

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There is no teachings in the specification to show the enablement of a starting factor VIII solution having a specific activity at least equal to 50 IU/mg (claim 44) or a starting factor VIII solution having a specific activity at least equal to 100 IU/mg (claim 45); a concentration of the starting factor VIII solution is from approximately 2 to approximately 100 IU/ml (claim 46) or a concentration of the starting factor VIII solution is from approximately 10 to approximately 50 IU/ml (claim 47); a protein content of the starting factor VIII solution is approximately 0.05 to approximately 0.5 mg/ml (claim 48)

or a protein content of the starting factor VIII solution is approximately 0.1 to approximately 0.5 mg/ml (claim 49). However, the specification does not enable a method of preparing a factor VIII solution, wherein the starting factor VIII solution having a specific activity at least equal to 50 IU/mg or 100 IU/mg or having a concentration from approximately 2 to approximately 100 IU/ml or from approximately 10 to approximately 50 IU/ml or a protein content from approximately 0.05 to approximately 0.5 mg/ml or from approximately 0.1 to approximately 0.5 mg/ml as claimed because there are no working examples or data or evidence in the instant specification, except for recitation the various unit ranges claimed in claims 44-49 (See e.g. page 8, lines 18 to 34 in the instant specification).

The specification teaches on Example 1 the preparation of a factor VIII solution by filtration from a cryoprecipitated fraction of plasma wherein the starting factor VIII solution is carried out in 835 g of cryoprecipitate, representing 113.5 liters of plasma, are redissolved in a solution of heparinized water (3 IU/ml). When one calculates 3 X 113.5 divided by 835, the result is approximately .47 IU/mg. Thus, according to Example 1 in the instant specification, the starting factor VIII solution has a specific activity of about .47 IU/mg and it is not clear how the starting factor VIII solution has specific activity at least equal to 50 IU/mg or 100 IU/mg as claimed in claims 44 and 45. Further, Table I, which is purified and filtered factor VIII has a specific activity of maximum 95 IU/mg, and maximum of protein content of 1.13 mg/ml. respectively. Therefore, the scope of the claims is not commensurate with the enablement provide by the disclosure with regard to a starting factor VIII solution having a specific activity at

least equal to 50 IU/mg or 100 IU/mg or having a concentration from approximately 2 to approximately 100 IU/ml or from approximately 10 to approximately 50 IU/ml or a protein content from approximately 0.05 to approximately 0.5 mg/ml or from approximately 0.1 to approximately 0.5 mg/ml as claimed in claims 44 to 49, respectively.

Thus, the scope of the specific activity, concentration and protein content of the starting factor VIII claimed are very broad and speculative, and as such, it would include those ranges that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine under what condition, the claimed invention as broadly claimed in claims 44-49 is enabled, since a wide range of starting factor VIII solution having a specific activity at least equal to 50 IU/mg or 100 IU/mg or having a concentration from approximately 2 to approximately 100 IU/ml or from approximately 10 to approximately 50 IU/ml or a protein content from approximately 0.05 to approximately 0.5 mg/ml or from approximately 0.1 to approximately 0.5 mg/ml are contemplated and are encompassed as well as various situations. The results desired appear to be highly dependent on all variables, the relationship of which are not clearly disclosed.

Therefore, without guidance through working example(s), one of ordinary skill in the art would not predict from the protocols disclosed on page 8, lines 18 to 33 in the instant specification to prepare a factor VIII solution, wherein the starting factor VIII solution has specific activities, concentrations and protein contents in the manner

claimed in claims 44-49 in the instant invention. Thus, the specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claims. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the invention.

CONCLUSION AND FUTURE CORRESPONDENCE

7. No claim is allowed, claims 24, 25, 36 and 37 are objected and claims 29, 31-34, 39-49 and 51 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached on (571) 272-0925. The appropriate fax phone number for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Jon P. Weber, Ph.D.
Primary Examiner

AM Mohamed/AAM

July 12, 2004